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BANNER & WITCOFF, LTD.
1100 13th STREET, N.W.
SUITE 1200
WASHINGTON, DC 20005-4051

EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT	PAPER NUMBER
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1634

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/073,123

Applicant(s)

LI ET AL.

Examiner

Jehanne S. Sitton

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 25 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,54,56-59 and 61-63 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 54, 56-59 and 61-63 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. Currently, claims 1, 3, 54, 56-59 and 61-63 are pending and under consideration in the instant application. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following contains new grounds rejection, as well as reiterated rejections. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is Non-FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The objections to the specification, made at sections 4 and 5 of the previous office action are withdrawn in view of the amendment to the drawings and the arguments presented at pages 7 and 8 of the response dated 1/25/2007.

4. The rejection of claims 1, 3, 57-59 and 61-63, under the enablement requirement of 35 USC 112/first paragraph made at section 8 of the previous office action is withdrawn in view of the amendment to the claims. Further, the arguments at the para bridging pages 11-12 are persuasive. The amendments to claim 1, however, have necessitated new grounds of rejection.

Claim Rejections - 35 USC § 112

5. Claims 54 and 56 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite “a WIP1 gene ... having a nucleotide sequence of nucleotides 1-1818 of SEQ ID NO: 1. The term “having” is considered open, for example, as “comprising”. This transitional terminology allows for additional elements on either side of the indicated SEQ ID NO:, but not additional sequences in the middle. However, the sequences of SEQ ID NO: 1 appears to be a coding sequences, without introns. However, a gene normally includes introns, and it appears that the WIP1 gene has introns (see previous dbSNP report, which designates exonic polymorphisms in reference to a genomic contig. The SNPs are spaced more than 2973 nucleotides apart, in different exons). Accordingly, it is unclear how a WIP1 gene can “comprise” or “have” the indicated SEQ ID NO, which are CDS and exclude introns, and still be a “gene”.

Response to Arguments

6. The response traverses the rejection. The response asserts that claim 1 has been amended to delete references to particular nucleotides. This argument has been thoroughly reviewed but was not found persuasive to overcome the rejection on claims 54 and 56. further, the arguments with regard to written description are not persuasive as the claims are rejected under 35 USC 112/2nd paragraph.

Written Description

7. Claims 1, 3, 54, and 56-59 and 60-63 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims have been amended to recite “detecting and measuring gene copy number of a WIP1 gene in a breast tissue...”. The designation of WIP1, however, includes a large genus of molecules, including mutants, variant, and homologs of SEQ ID NO: 1 and SEQ ID NO: 3, as exemplified by the definition in the specification. The specification defines “WIP1” as nucleic acid which can include their polymorphic variants, alleles, mutants that have substantial nucleotide sequence homology with the nucleotide sequence of GenBank entry AAB61637 or “substantial” nucleotide sequence homology with the nucleotide sequence as set forth in SEQ ID NO 1 (para bridging pages 21 and 22 of the specification). Although the specification does not provide an express definition for substantial nucleotide sequence homology in the context of nucleic acids, at page 21, the specification provides a broad definition with regard to protein homology as having only 60% identity. Therefore, it is clear that the term “substantial” allows for a large degree of variability when comparing two sequences. Accordingly, it is clear from the guidance in the specification that the term “WIP1” is not limited to the gene which encodes the SEQ ID NO: 1 transcript, but also broadly encompass mutants, allelic variants, and homologs. However, the specification only teaches the sequence of SEQ ID NO: 1 and 3, which correspond to WIP 1 coding sequence. Neither sequence is the sequence of the WIP1 gene, nor

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the rejection is maintained as the specification does not provide support for a gene with the sequence of SEQ ID NO 1.

Enablement

9. Claims 1, 3, 54, 56-59 and 61-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of diagnosing breast cancer in a human comprising detecting and measuring gene copy number of the WIP1 gene which encodes the transcript of SEQ ID NO: 1 in a breast tissue sample from the human that is suspected to be cancerous, thereby generating data for a test gene copy number and comparing the test gene copy number to data for a control gene copy number, wherein amplification of the gene in the breast tissue sample relative to the control indicates the presence of breast cancer in the human, does not reasonably provide enablement for a method a method of diagnosing breast cancer in a human comprising detecting and measuring gene copy number of any "WIP1" gene in a breast tissue sample from the human that is suspected to be cancerous, thereby generating data for a test gene copy number and comparing the test gene copy number to data for a control gene copy number, wherein amplification of the gene in the breast tissue sample relative to the control indicates the presence of breast cancer in the human. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

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is it representative of the broad genus of mutants, variants, and especially homologs of WIP 1 with altered structure or function, as well as occurring at a different region of the human chromosome, let alone chromosome 17. Based on the broad definition of the WIP1 gene (nucleic acid sequences that have substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry AAB61637 or SEQ ID NO:1), the large genus of WIP1 genes recited in the instant claims encompasses structurally and functionally distinct molecules, which have not been taught or described in the specification, whose amplification would not necessarily be expected to be associated with breast cancer. Further, with regard to claims 54 and 56, the specification does not teach a gene comprising the sequence of SEQ ID NO: 1. The term “having” is considered open, for example, as “comprising”. This transitional terminology allows for additional elements on either side of the indicated SEQ ID NO:, but not additional sequences in the middle. However, the sequences of SEQ ID NO: 1 appears to be a coding sequences, without introns. However, a gene normally includes introns, and it appears that the WIP1 gene has introns (see previous dbSNP report, which designates exonic polymorphisms in reference to a genomic contig. The SNPs are spaced more than 2973 nucleotides apart, in different exons). However, the specification does not teach a gene which “comprise” or “has” the indicated SEQ ID NO, which is a CDS and excludes introns.

Response to Arguments

8. The response traverses the rejection. The grounds of rejection with regard to the originally filed specification not providing support for SEQ ID NO: 1 are withdrawn in view of the explanation given at page 10 of the response (first para). With regard to claims 54 and 56,

“Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.”

The nature of the invention and the breadth of the claims:

The claims are drawn to a method of diagnosing breast cancer in a human comprising detecting and measuring gene copy number of any “WIP1” gene in a breast tissue sample from the human that is suspected to be cancerous, thereby generating data for a test gene copy number and comparing the test gene copy number to data for a control gene copy number, wherein amplification of the gene in the breast tissue sample relative to the control indicates the presence of breast cancer in the human.

The invention is in a class of inventions which the CAFC has characterized as ‘the unpredictable arts such as chemistry and biology’ (*Mycolgen Plant Sci., Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330 (Federal Circuit 2001)).

The amount of direction or guidance:

The claims have been amended to recite “detecting and measuring gene copy number of a WIP1 gene in a breast tissue...”. The specification teaches that WIP1 is a serine/threonine specific protein phosphatase type 2C (PP2C) family member whose expression is induced in response to gamma or UV radiation in a p53-dependent manner (pages 37 and 38). The designation of WIP1, however, includes a large genus of molecules, including mutants, variant, and homologs of SEQ ID NO: 1 and SEQ ID NO: 3, as exemplified by the definition in the

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specification. The specification defines “WIP1” as nucleic acid which can include their polymorphic variants, alleles, mutants that have substantial nucleotide sequence homology with the nucleotide sequence of GenBank entry AAB61637 or “substantial” nucleotide sequence homology with the nucleotide sequence as set forth in SEQ ID NO 1 (para bridging pages 21 and 22 of the specification). Although the specification does not provide an express definition for substantial nucleotide sequence homology in the context of nucleic acids, at page 21, the specification provides a broad definition with regard to protein homology as having only 60% identity. Therefore, it is clear that the term “substantial” allows for a large degree of variability when comparing two sequences. Accordingly, it is clear from the guidance in the specification that the term “WIP1” is not limited to the gene which encodes the SEQ ID NO: 1 transcript, but also broadly encompass mutants, allelic variants, and homologs. However, the specification only teaches the sequence of SEQ ID NO: 1 and 3, which correspond to WIP 1 coding sequence. Neither sequence is the sequence of the WIP1 gene, nor is it representative of the broad genus of mutants, variants, and especially homologs of WIP 1 with altered structure or function, as well as occurring at a different region of the human chromosome, let alone chromosome 17. Based on the broad definition of the WIP1 gene (nucleic acid sequences that have substantial nucleotide sequence homology with the nucleotide sequence of the GenBank entry AAB61637 or SEQ ID NO:1), the large genus of WIP1 genes recited in the instant claims encompasses structurally and functionally distinct molecules, which have not been taught or described in the specification, whose amplification would not necessarily be expected to be associated with breast cancer.

Further, with regard to claims 54 and 56, the specification does not teach a gene comprising the sequence of SEQ ID NO: 1. The term “having” is considered open, for example,

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as “comprising”. This transitional terminology allows for additional elements on either side of the indicated SEQ ID NO:, but not additional sequences in the middle. However, the sequences of SEQ ID NO: 1 appears to be a coding sequences, without introns. However, a gene normally includes introns, and it appears that the WIP1 gene has introns (see previous dbSNP report, which designates exonic polymorphisms in reference to a genomic contig. The SNPs are spaced more than 2973 nucleotides apart, in different exons). However, the specification does not teach a gene which “comprise” or “has” the indicated SEQ ID NO, which is a CDS and excludes introns.

Presence and absence of working examples:

The specification teaches that the WIP1 gene is amplified and/or overexpressed in several breast tumor cell lines (Table 1). The specification also teaches that the WIP1 gene is overexpressed in several primary tumor samples of different types of cancer and amplified in several primary breast tumor samples (Table 2). The specification further teaches methods for detecting and quantitating WIP1 gene amplification and level of expression (pages 40-45). At page 64, the specification teaches a working example of detecting WIP1 amplification using microarray based CGH (comparative genomic hybridization). The specification teaches using a TaqMan probe set representing the target and a reference probe representing normal non amplified, single copy region in the genome. At page 66, the specification teaches that the inventors demonstrated that WIP1 is located at the epicenter of the amplification region using Q-PCR and fluorogenic TaqMan probes based on undisclosed EST's or BAC sequences. The specification, however, does not teach any working examples of diagnosing breast cancer in

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humans by detecting amplification of any WIP1 gene homologs, as is broadly encompassed by the claims.

The state of the prior art and the predictability or unpredictability of the art:

With regard to an association of the amplification of homolog variants of the WIP1 gene with cancer, Lavi et al. teach that PP2Calpha was expressed at lower levels in 7 out of 8 colorectal tumors compared to adjacent normal colon tissues, suggesting that amplification of the PP2Calpha homolog of the WIP1 gene is not associated with cancer (see Lavi et al., WO97/10796, page 46, lines 19-22).

The level of skill in the art:

The level of skill in the art is deemed to be high.

The quantity of experimentation necessary:

Based on the lack of guidance in the specification and the unpredictability in the art, it would require undue experimentation for the skilled artisan to practice the invention as broadly as it is claimed. The skilled artisan would be required to test a large number of patients and controls to determine whether an association existed between amplification of WIP1 homologs and breast cancer in humans. Such experimentation would be replete with trial and error analysis as there is no indication from the specification, that amplification of WIP1 homologs on different regions of the human genome, are associated with breast cancer. Given that the region the WIP gene resides in is known to be amplified in breast cancer, it is not clear whether the

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association is due to amplification of WIP1 or another gene in the amplified region. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one skilled in the art to perform the methods of the instant claims as written.

In the interest of compact prosecution, the following rejections are set forth.

Claim Rejections - 35 USC § 102

10. Claims 1, 3, 54, 56, 57, 61, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Kallioniemi et al. (herein referred to as Kallioniemi, *Proc. Natl. Acad. Sci. USA*, vol. 91, pages 2156-2160, 03/1994), as defined by Wu et al. (herein referred to as Wu, *Cancer Res.*, vol. 61, pages 4951-4955, 07/2001) and Genbank Accession number NM_003620 (1999, as set forth at pages 36-37 of the instant specification).

It is noted that the recitation of "...a nucleotide sequence of SEQ ID NO..." encompasses sequences from within the recited SEQ ID NO. in contrast to the recitation of "the nucleotide sequence of..."

Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 (see Figure 1 of Wu).

Kallioniemi teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell

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lines (instant claim 1; see Tables 1 and 2, page 2156, all of paragraph 5, and page 2157, all of paragraphs 1 and 2). Kallioniemi teach that copy number increases of the 17q22-24 region were found in 18% of primary breast tumors and 67% of breast cancer cell lines examined (see Tables 1 and 2 and page 2159, paragraph 2, lines 5 and 6 of Kallioniemi). This above method taught by Kallioniemi involves comparative genomic hybridization in which the relative intensity of a fluorescent signal from a test chromosome (from tumor cells for example) hybridized with a labeled probe is compared to the intensity of a fluorescent signal from a control chromosome hybridized with the same probe that emits a different fluorescent color (instant claims 1, 54, 56, 57, 61, and 62; see page 2156, paragraph 2, lines 3-8 of Kallioniemi). Kallioniemi teaches that the probe/chromosome hybridizations of the above method were analyzed using a digital image analysis system that was based on either a Nikon SA or Zeiss Axioplan microscope equipped with a cooled charge-coupled device camera and a filter system consisting of a triple-band-pass beam splitter and emission filters and therefore the data was stored in an electronic video format (instant claim 3; see Figure 1 and page 2157, paragraph 3, lines 1-6 of Kallioniemi). Kallioniemi further teaches that three-color images derived from the above method were processed with a Sun IPX workstation using Scil-Image software for pseudocolor display and therefore the data was analyzed via video display and compared and compiled at a location where the data was transmitted (instant claim 3; page 2157, paragraph 3, lines 11-14 of Kallioniemi).

Although Kallioniemi does not teach the sequence which is amplified, nor does Wu teach the specific sequence detected by Kallioniemi, as stated in the MPEP in chapter 2100:

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the instant case, Kallioniemi teaches detecting amplification of 17q22-24 in a number of different tumors and cell lines. Thus, the office has sound basis for believing that some breast tumor samples which showed amplification of 17q22-q24 contained the gene which encoded the claimed sequences.

Response to Arguments

11. The response traverses the rejection, and notes that claim 2 was previously canceled. This is acknowledged, the designation of claim 2 instead of claim 3 was a typographical error. The rejection, however, specifically pointed to teachings in the reference with regard to claim 3. The response asserts that Kallioniemi does not teach each element as recited in claim 1 and provides absolutely no guidance for associating amplification of any of the genes located within 17q22-24 region with a breast cancer, let alone a disclosure associating amplification of WIP1 with breast cancer, and thus does not anticipate the claims. This argument has been thoroughly reviewed but was not found persuasive. The claims only require detecting and measuring gene copy number of a WIP1 gene in a breast tissue and comparing it to a control gene copy number. As set forth in the rejection above, Kallioniemi teaches detecting amplification of 17q22-24 in a number of different breast tumors using CGH to provide a test copy number and comparison to a control copy number. Although Kallioniemi does not appreciate that WIP1 is in the region found to be amplified, this is an inherent property of the region taught by Kallioniemi as evidenced by Wu. Further, the fact that Wu was published after the filing date, does not overcome it's use to establish that WIP1 is within this region. Wu was not used as prior art under 35 USC 102, but rather as evidence. As set forth in the MPEP, 2131.01:

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To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence... Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999) (Two prior art references disclosed blasting compositions containing water-in-oil emulsions with identical ingredients to those claimed, in overlapping ranges with the claimed composition. The only element of the claims arguably not present in the prior art compositions was “sufficient aeration . . . entrapped to enhance sensitivity to a substantial degree.” ... Also note that the critical date of extrinsic evidence showing a universal fact need not antedate the filing date.

Accordingly, the rejection set forth above, is maintained.

12. Claims 1, 3, 54, 56, 57, 59, 61, and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Orsetti (Orsetti et al; *Oncogene*, vol. 18, pages 6262-6270, 1999), as defined by Wu et al. (herein referred to as Wu, *Cancer Res.*, vol. 61, pages 4951-4955, 07/2001) and Genbank Accession number NM_003620 (1999, as set forth at pages 36-37 of the instant specification).

It is noted that the recitation of “...a nucleotide sequence of SEQ ID NO...” encompasses sequences from within the recited SEQ ID NO. in contrast to the recitation of “the nucleotide sequence of...”

Wu teaches that the human WIP1 gene is located in the 17q22-23 region of chromosome 17 (see Figure 1 of Wu).

Orsetti teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors, and 3 of the entire long arm (see Fig. 2, Fig 5, and para bridging cols 1 and 2 of page 6264). The method

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taught by Orsetti includes PCR, FISH, and CGH (see page 6269). Orsetti teaches microscopy and digital image analysis (page 6269, fig 4; claim 3).

Although Orsetti does not teach the specific nucleotide sequence which is amplified, as stated in the MPEP in chapter 2100:

Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

In the instant case, Orsetti teaches detecting amplification of 17q21-24 and 17q21-qter in a number of different breast tumors and cell lines. Thus, the office has sound basis for believing that some breast tumor samples which showed amplification of 17q21-q24 and 17q21-qter contained the gene which encoded the claimed sequences.

Response to Arguments

13. The response traverses the rejection, and notes that claim 2 was previously canceled. This is acknowledged, the designation of claim 2 instead of claim 3 was a typographical error. The rejection, however, specifically pointed to teachings in the reference with regard to claim 3. The response asserts that the rejection relies on Orsetti's generic disclosure and that Orsetti does not provide guidance for associating amplification of any of the genes located within 17q21-24 region with a breast cancer, let alone a disclosure associating amplification of WIP1 with breast cancer, and thus does not anticipate the claims. This argument has been thoroughly reviewed but was not found persuasive. The claims only require detecting and measuring gene copy number of a WIP1 gene in a breast tissue and comparing it to a control gene copy number, wherein the

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amplification is indicates the presence of a breast cancer. As set forth in the rejection above, Orsetti teaches detecting amplification of 17q21-24 in a number of different breast tumors using CGH and FISH to provide a test copy number and comparison to a control copy number, wherein amplification is indicative of a breast cancer. At Figure 2, Orsetti teaches amplification of a region of chromosome 17q21-24 which includes the WIP1 gene (see lanes 15-18, marker rows D17S604-D17S1855). Although Orsetti does not appreciate that WIP1 is in the region found to be amplified, this is a property of the region taught by Orsetti as evidenced by Wu. Further, the fact that Wu was published after the filing date, does not overcome it's use to establish that WIP1 is within this region. Wu was not used as prior art under 35 USC 102, but rather as evidence. As set forth in the MPEP, 2131.01:

To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence... Note that as long as there is evidence of record establishing inherency, failure of those skilled in the art to contemporaneously recognize an inherent property, function or ingredient of a prior art reference does not preclude a finding of anticipation. *Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1948 (Fed. Cir. 1999) (Two prior art references disclosed blasting compositions containing water-in-oil emulsions with identical ingredients to those claimed, in overlapping ranges with the claimed composition. The only element of the claims arguably not present in the prior art compositions was "sufficient aeration . . . entrapped to enhance sensitivity to a substantial degree." ... Also note that the critical date of extrinsic evidence showing a universal fact need not antedate the filing date.

Accordingly, the rejection set forth above, is maintained.

Claim Rejections - 35 USC § 103

14. Claim 58 is rejected under 35 USC 102(a) as being unpatentable over Orsetti in view of Backman (Backman et al; US Patent 5,516,663).

Orsetti teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors, and 3 of the entire long arm (see Fig. 2, Fig 5, and para bridging cols 1 and 2 of page 6264). The method taught by Orsetti includes PCR (page 6269). Orsetti does not teach amplification using LCR, however, Backman teaches amplification of targets using LCR (see col. 2). Additionally, it was known in the art at the time the invention was made that LCR was a suitable method of amplification (acknowledged in the specification, page 43). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the invention was made to use LCR in the method of Orsetti in view of the teachings of Backman. The ordinary artisan would have been motivated to use LCR in the method of Orsetti because it was known in the art at the time the invention was made that LCR was an equivalent method of amplification for target detection.

15. Claim 63 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kallioniemi or Orsetti, each in view of Pinkel (Pinkel et al; Nature Genetics, vol. 20, pages 207-211, 1998).

Kallioniemi teach a method of detecting and measuring DNA sequence copy number increases for the 17q22-24 region in several human primary breast tumors and breast cancer cell lines (instant claims 1 and 2; see Tables 1 and 2, page 2156, all of paragraph 5, and page 2157, all of paragraphs 1 and 2). Kallioniemi teach that copy number increases of the 17q22-24 region were found in 18% of primary breast tumors and 67% of breast cancer cell lines examined (see Tables 1 and 2 and page 2159, paragraph 2, lines 5 and 6 of Kallioniemi). This above method taught by Kallioniemi involves comparative genomic hybridization in which the relative intensity of a fluorescent signal from a test chromosome (from tumor cells for example)

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hybridized with a labeled probe is compared to the intensity of a fluorescent signal from a control chromosome hybridized with the same probe that emits a different fluorescent color (instant claims 1, 54, 56, 57, 61, and 62; see page 2156, paragraph 2, lines 3-8 of Kallioniemi).

Orsetti teaches a method of detecting and measuring DNA sequence copy number increases over the entire 17q21-q24, including 17q21-qter, in 15 human breast tumors, and 3 of the entire long arm (see Fig. 2, Fig 5, and para bridging cols 1 and 2 of page 6264). This above method taught by Orsetti uses CGH (see page 6269).

Neither Kallioniemi nor Orsetti teach using microarray based CGH, however Pinkel teaches that arrays allow for high resolution analysis of DNA copy number variation using CGH. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Kallioniemi or Orsetti with the microarray based CGH method of Pinkel. The ordinary artisan would have been motivated to improve the CGH methods of Kallioniemi or Orsetti with the microarray based method of Pinkel for higher resolution analysis of DNA copy number variations.

Conclusion

16. No claims are allowed.
17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached on (571) 272-0735. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton
Primary Examiner
Art Unit 1634

4/13/07